REMARKS

Claim Amendments

Claims 26 and 28-29, 34-35 and 71-72 are pending herein. New Claims 71-72 have been added herein to reintroduce previous cancelled subject matter. New Claims 71-72 are withdrawn herein. Support for new Claims 71-72 can be found throughout the specification and in the claims as originally filed. No new matter has been added.

Telephonic Interview

Applicants would like to thank Examiner Blanchard for taking the time to participate in a telephonic interview on February 17, 2009. The amendments and remarks herein reflect the substance of the discussion.

Rejection of Claims 26, 28-29, and 34-35 Under 35 U.S.C. 112, First Paragraph

Claims 26, 28-29, and 34-35 are currently rejected as failing to meet the written description requirement. Applicants respectfully traverse this rejection.

To determine whether the written description requirement has been met, it is necessary to determine what was already in the art, as well as Applicants' contribution to the art of oligonucleotide based immunostimulatory compounds.

As stated previously in the Response filed with the USPTO on December 4, 2008, the cited art already taught that bacterial DNA and synthetic oligodeoxynucleotides containing unmethylated CpG dinucleotides induce an immune response. Additionally, at the time the invention was filed, it was also know that CpG-containing oligonucleotides lost stimulatory activity if the CpG was eliminated or if the cytosine was replaced by 5'-methylcytosine (in contrast to 5'-methylation of other cytosines which did not reduce activity). Thus, the CpG dinucleotide is the sole structural requirement to generate the immune response.

Applicants' contribution to that art was the surprising discovery that replacement of cytosine (C) in a CpG dinucleotide of an immunostimulatory CpG-containing oligonucleotide by cytosine ananlogue (C*), in particular 5-hydroxycytosine, 5-hydroxymethylcytosine, N4-alkylcytosine, arabinocytosine or 4-thiouracil, does not abolish the immune stimulatory properties of the oligonucleotide. In other words, if a given CpG-containing oligonucleotide is

immunostimulatory, its sequence will remain immunostimulatory (and perhaps be improved) with Applicants' modification in Applicants' claimed method.

The Office Action goes to great lengths to describe all the possible modifications that one skilled in the art could do to a CpG-containing oligonucleotide to further alter the immunostimulatory properties of the CpG-containing oligonucleotide. However, that is not relevant to the claim as changes outside the CpG dinucleotide are not required by the claim. Furthermore, while Applicants acknowledge that changes outside of the CpG motif can be made to the CpG-containing oligonucleotide; these changes alone are not enough as an active CpG motif is required. Once a CpG motif loses activity (e.g., by replacement of the C with 5'-methylcytosine), no modifications to the oligonucleotide outside the CpG motif such as those relied upon by the Office Action, whether it is length, sequence or backbone modifications, will cause this oligonucleotide to regain activity. However, by replacing the 5'-methylcytosine, in this example, with one of the instantly claimed C*s, the oligonucleotide would regain its immunostimulatory activity.

Thus, Applicants' contribution was not the modification of a particular CpG-containing oligonucleotide sequence. Rather, one skilled in the art would recognize Applicants' contribution that, all things being equal, the replacement of cytosine in a CpG dinucleotide of any immunostimulatory CpG-containing oligonucleotide by the various claimed cytosine analogues would not abolish the immunostimulatory activity of any such oligonucleotide.

In summary, Applicants' respectfully submit that when what was known in the art at the time of Applicants' filing, and Applicants' contribution to the art is also properly considered, it becomes readily apparent that the written description is satisfied in the present case. On this basis alone, Applicants respectfully request that this rejection be withdrawn. However, for purposes of a complete record for any appeal, if necessary, Applicants challenge the PTO's assertion that the specification only sets for a single immunostimulatory oligonucleotide.

The Office Action continues to assert that the specification only sets forth a single immunostimulatory oligonucleotide (i.e., 5-CTATCTGACGTTCTCTGT-3') comprising the formula C*pG, wherein C* is 5'-hydroxycytosine, 5'-hydroxymethylcytosine or N4-ethylcytosine, that stimulates an immune response. Applicants respectfully disagree. A correct reading of this teaching within the specification would show that the specification sets forth six (6) immunostimulatory oligonucleotides (i.e., 5-CTATCTGACGTTCTCTGT-3'; 5-

CTATCTGAC*GTTCTCTGT-3', C* = 5'-hydroxycytosine; 5-CTATCTGAC*GTTCTCTGT-3', C* = 5'-hydroxymethylcytosine; 5-CTATCTGAC*GTTCTCTGT-3', C* = N4-ethylcytosine; 5-CTATCTGAC*GTTCTCTGT-3', C* = arabinocytosine; and 5-CTATCTGAC*GTTCTCTGT-3', C* = 4-thiouracil). Each sequence is its own, independent species and, although each sequence shares the characteristic of being able to generate an immune response, the success of one C* is not predictive of whether a different C* would also be recognized by the TLR9 protein receptor, thereby being capable of generating an immune response. For example, U.S. patent publication 20030036516 teaches several C* modifications of the CpG motif that result in the abolishment of the immunostimulatory activity of this motif.

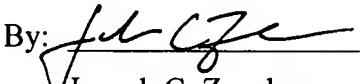
The instant specification teaches several C* analogues that can be substituted for the C in a CpG motif and the CpG-containing oligonucleotide will remain immunostimulatory. As such, it would be clear to one skilled in the art that the Applicants, at the time the application was filed, had possession of the claimed invention. Reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner believes that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

Dated: April 17, 2009

By: 
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